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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,811	04/08/2004	Suketu P. Sanghvi	P0453.70115US01	9061

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EXAMINER	
JAGOE, DONNA A	
ART UNIT	**PAPER NUMBER**
1614	

MAIL DATE	DELIVERY MODE
01/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,811	SANGHVI ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,8,10,17-19,22,26,33-39,44,50,54-56,58,61-68,71-73,77,78,83-86,92-94,101-103,106,110,117-121,129,133,136,140-144,147,149,155,158,163-165,172,176,179,180,183,187-189,195,196,202,206-208,214,216,219,221,223,225,228,231,232,235-247,252,255-257,261,267,271-283,285,287,289,291,293,294,296,299,302-304 and 307-315* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,7,8,10,17-19,22,26,33-39,44,50,54-56,58,61-68,71-73,77,78,83-86,92-94,101-103,106,110,117-121,129,133,136,140-144,147,149,155,158,163-165,172,176,179,180,183,187-189,195,196,202,206-208,214,216,219,221,223,225,228,231,232,235-247,252,255-257,261,267,271-283,285,287,289,291,293,294,296,299,302-304 and 307-315* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1, 7, 8, 10, 17-19, 22, 26, 33-39, 44, 293 and 294, drawn to a pharmaceutical preparation comprising a solution of methylnaltrexone, classified in class 514, subclass 282.

II. Claims 50, 54-56, 58 and 61-65, drawn to a method of preparing an autoclaved pharmaceutical preparation that has a concentration of methylnaltrexone degradation products not exceeding 2% and a pH of 4.25 or less, classified in class 514, subclass 282 and class 422, subclass 25.

III. Claims 66-68, 71-73, 77, 78 and 83-85 drawn to a method for preparing an autoclaved pharmaceutical preparation that has a concentration of methylnaltrexone degradations products not exceeding 2% and further comprising a chelating agent, classified in class 514, subclass 282.

IV. Claims 86, 92-94, 101-103, 106, 110, 117-121, 129, 133, 136, 140-144, 147, 149, 155, 158, m163-165, 172, 176, 179, 180, 183, 184, 187, 296 and 299, drawn to a pharmaceutical preparation comprising a solution of methylnaltrexone or salt thereof wherein the preparation after storage at about room temperature for six months has a concentration of

methylnaltrexone degradation not greater than 2%, classified in class 514, subclass 282.

V. Claims 188, 189, 195, 196, 202, 206-208, 214, 216, 219, 221, 223, 225, and 228, drawn to a pharmaceutical preparation comprising a solution of methylnaltrexone or salt thereof wherein the solution further comprises a chelating agent and after autoclaving the concentration of methylnaltrexone degradation products does not exceed 0.5%, classified in class 514, subclass 282.

VI. Claims 231-232, and 235-246, drawn to a pharmaceutical preparation comprising a solution of methylnaltrexone or salt thereof and at least one methylnaltrexone degradation inhibiting agent selected from the group consisting of a chelating agent, a buffering agent and antioxidant and combinations thereof wherein the solution has a pH ranging from 2 to 6 and substantially free of methylnaltrexone degradation products, classified in class 514, subclass 282.

VII. Claims 247, 252 and 255, drawn to a method of inhibiting the formation of methylnaltrexone degradation products in a pharmaceutical preparation comprising at least one of a chelating agent, a buffering agent, an antioxidant and combinations thereof and dissolving a powdered source of methylnaltrexone with a solution, classified in class 514, subclass 282.

VIII. Claims 256, 257, 261, 267, 271-282, drawn to a method of preparing a stable pharmaceutical preparation comprising an aqueous solution of

methylnaltrexone or salts thereof comprising processing the solution under at least one sterilization technique prior to and/or after terminal filling the solution in a sealable container and the **pH adjusting agent is excluded,** classified in class 514, subclass 282.

IX. Claims 283, 285, 287, 289, 291, drawn to a product comprising a stable lyophilized formulation of methylnaltrexone whereupon the formulation reconstitutes with water to a concentration of 20 mg/ml and has a pH of between 2 and 6, classified in class 514, subclass 282.

X. Claims 302-304, drawn to a product comprising methylnaltrexone in a concentration of 20 mg/ml and a degradation inhibiting agent selected from the group consisting of a chelating agent, a buffering agent, an antioxidant and combinations thereof, classified in class 514, subclass 282.

XI. Claims 307-315, drawn to a pharmaceutical preparation comprising methylnaltrexone; sodium chloride, citric acid, trisodium citrate and disodium edetate, classified in class 514, subclass 282.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be

entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejections are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

The inventions are distinct, each from the other because of the following reasons:

Inventions II and I are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the process as claimed can be used to make another and materially different product. See, Liebert et al., U.S. Patent No. 5,256,154.

Inventions II and III are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the subcombination requires the inclusion of a chelating agent. The examiner has required restriction between combination and subcombination inventions. Where applicant elects a subcombination, and claims thereto are subsequently found allowable, any claim(s) depending from or otherwise requiring all the limitations of the allowable subcombination will be examined for patentability in accordance with 37 CFR 1.104. See MPEP § 821.04(a). Applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present

application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Inventions III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions have different effects in that the group IV invention requires that after storage at about room temperature for six months has a concentration of methylnaltrexone degradation not greater than 2%.

Inventions IV and V are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the group IV invention does not require the inclusion of a chelating agent. The examiner has required restriction between combination and subcombination inventions. Where applicant elects a subcombination, and claims thereto are subsequently found allowable, any claim(s) depending from or otherwise requiring all the limitations of the allowable subcombination will be examined for patentability in accordance with 37 CFR 1.104. See MPEP § 821.04(a). Applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to

provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Inventions V and VI are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the group V invention does not require the inclusion of a buffering agent and antioxidant and is substantially free of degradation products of methylnaltrexone. The examiner has required restriction between combination and subcombination inventions. Where applicant elects a subcombination, and claims thereto are subsequently found allowable, any claim(s) depending from or otherwise requiring all the limitations of the allowable subcombination will be examined for patentability in accordance with 37 CFR 1.104. See MPEP § 821.04(a). Applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Inventions I-VI, VIII-XI and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant

case, the different inventions modes of operation in that the group VII requires the method of inhibiting the formation of methylnaltrexone degradation products in a pharmaceutical preparation comprising at least one of a chelating agent, a buffering agent, an antioxidant and combinations thereof and dissolving a powdered source of methylnaltrexone with a solution, not required by the groups I-VI and VIII-XI inventions.

Inventions II, III and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions have different designs in that the Group VIII invention specifically excludes the pH adjusting agent.

Inventions IX and X are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the group IX invention does not require the chelating agent, a buffering agent, an antioxidant. The examiner has required restriction between combination and subcombination inventions. Where applicant elects a subcombination, and claims thereto are subsequently found allowable, any claim(s) depending from or otherwise requiring all the limitations of the allowable subcombination will be examined for patentability in accordance with 37 CFR 1.104. See MPEP § 821.04(a). Applicant is advised that if any claim presented in a

continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Inventions X and XI are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the Group XI requires the presence of chloride, citric acid, trisodium citrate and disodium edetate, that is not required in the Group X invention. The examiner has required restriction between combination and subcombination inventions. Where applicant elects a subcombination, and claims thereto are subsequently found allowable, any claim(s) depending from or otherwise requiring all the limitations of the allowable subcombination will be examined for patentability in accordance with 37 CFR 1.104. See MPEP § 821.04(a). Applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required

because the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

Claims 1, 7, 8, 10, 17-19, 22, 26, 33-39, 44, 50, 54-56, 58, 61, 62-68, 71-73, 77, 78, 83-86, 92-94, 101-103, 106, 110, 117-121, 129, 133, 136, 140-144, 147, 149, 155, 158, 163-165, 172, 176, 179, 180, 183, 184, 187-189, 195, 196, 202, 206-208, 214, 216, 219, 221, 223, 225, 228, 231, 232, 235-247, 252, 255-257, 261, 267, 271-283, 285, 287, 289, 291, 293, 294, 296, 299, 302-304 and 307-315 are generic to the following disclosed patentably distinct species:

A. chelating agent

B. buffering agent

C. antioxidant

D. isotonicity agent

E. opioid

F. cryoprotective agent.

The species are independent or distinct because they are unrelated. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

A telephone call to the attorney is not required where: 1) the restriction requirement is complex, 2) the application is being prosecuted pro se, or 3) the examiner knows from past experience that a telephone election will not be made, see MPEP Sect. 812.01.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions

unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe
Patent Examiner
Art Unit 1614

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